Complete and Durable Response of Choroid Metastasis from Non-small Cell Lung Cancer with Systemic Bevacizumab and Chemotherapy

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Abstract: Ocular metastasis from lung cancer is uncommon. We report a patient with metastatic non-small cell lung cancer who was found to have a metastatic lesion in the choroid at the time of presentation. The patient was treated with carboplatin, gemcitabine, and bevacizumab. After three cycles of chemotherapy, radiologic imaging and ophthalmologic examination demonstrated complete resolution of the choroid lesion. This case report demonstrates the durable response of choroidal metastasis from non-small cell lung cancer to systemic bevacizumab and chemotherapy.

Key words: Choroid metastasis, Non small cell lung cancer, Bevacizumab.

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A 42-year-old woman with newly diagnosed metastatic non-small cell lung cancer (poorly differentiated large cell carcinoma) presented with 1 week history of blurred vision in her right eye and metamorphopsia where flat surfaces appeared curved. A computerized tomography scan of the neck and chest performed at initial presentation had revealed multiple left pulmonary masses, a right upper lobe lesion as well as enlarged left anterior cervical, bilateral supraclavicular, mediastinal, prevascular, paratracheal, and subcarinal lymph nodes. Pathologic diagnosis of poorly differentiated large cell carcinoma was obtained from core-needle biopsy of the left anterior cervical lymph node. Brain magnetic resonance imaging revealed a metastatic lesion in the choroid of the right globe (Figure 1*A*). Ophthalmology evaluation of the right fundus showed a 12 × 12 mm amelanotic choroidal tumor at the fovea and temporal macula with overlying subretinal fluid and an associated inferior exudative retinal detachment (Figure 1*B*). Tumor height was 6.3 mm with high internal reflectivity on ocular echography.

Systemic chemotherapy was initiated. After her first cycle of carboplatin, gemcitabine, and bevacizumab, she experienced improvement in visual symptoms. Magnetic resonance imaging after cycle 3 of chemotherapy showed complete resolution of the choroid lesion (Figure 2*A*), coinciding with improvement in her vision (Figure 2*B*) and disease response systemically. Subsequently, she completed six cycles of chemotherapy and attained a partial response in her lung mass. At the time of this report she was alive with normal vision and receiving her seventh maintenance dose of every 3 week bevacizumab without experiencing systemic or ocular toxicity.

DISCUSSION

The highly vascular uveal tract is the most common part of the eye involved by metastases.[1] Within the uvea, the choroid (88%) is the most commonly affected site followed by the iris (9%) and ciliary body (2%).[2] Breast and lung cancers are the predominant tumors to metastasize to the uvea,[2,3] and between 67 and 88% of patients have metastatic lesions elsewhere at the time of diagnosis of ocular involvement.[4]

Although fine-needle aspiration biopsy can be used to establish the diagnosis; the choroidal tumor characteristics, presence of distant metastases, and patient history were sufficient to infer the diagnosis of choroidal metastasis in this case.

Treatment for orbital and ocular adnexal metastases is palliative because the presence of such metastases suggests hematogenous spread of cancer. In line with this, the aims for treatment are to maximize quality of life, and restore or preserve vision. This may be achieved with either radiotherapy or chemotherapy. Surgery has not played an important role (other than diagnostic biopsy, if needed) as surgery carries great potential morbidity and often there is no need for tumor debulking.

External beam radiotherapy in the range of 20 to 50 Gy has been commonly used[5] and achieves symptom relief although controlling tumor growth. This modality is particularly applicable for large tumors that involve the optic nerve/macula and cause substantial visual disturbance. Visual preservation after external beam radiotherapy may be only for the short-term because potential long-term side effects include cataract formation and radiation retinopathy.[5] Radioac-

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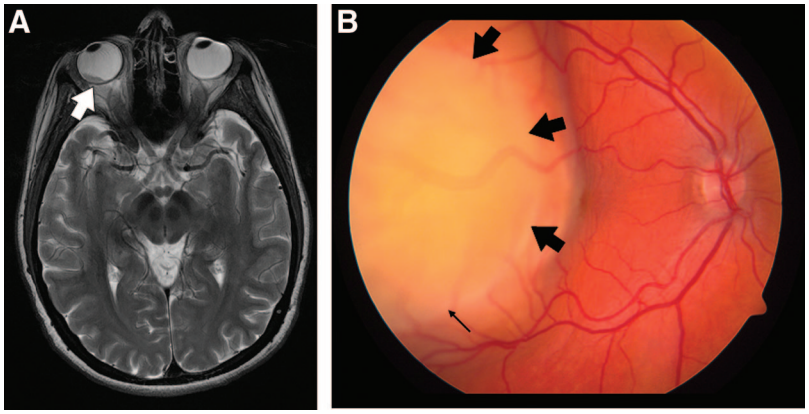

FIGURE 1. *A,* Magnetic resonance imaging (MRI) brain at presentation revealing a metastatic lesion in the choroid of the right globe (white block arrow). *B,* Ophthalmology evaluation of the right fundus showing a 12 × 12 mm amelanotic choroidal tumor at the fovea and temporal macula (black block arrow) with overlying subretinal fluid and an associated inferior exudative retinal detachment (black line arrow).

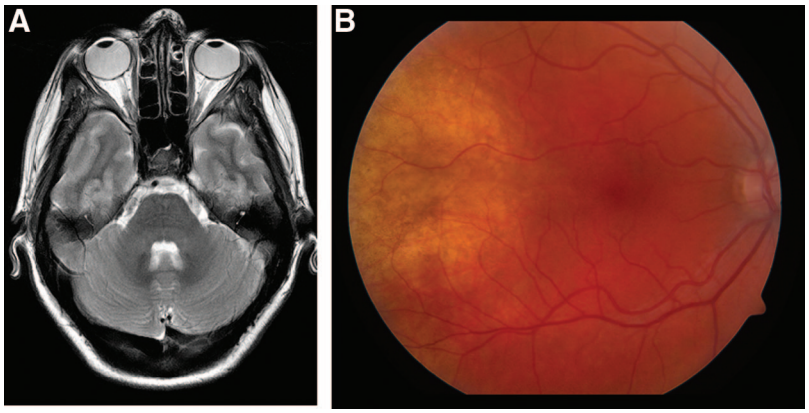

FIGURE 2. *A,* Magnetic resonance imaging (MRI) brain after three cycles of chemotherapy showing complete resolution of the choroid lesion. *B,* Ophthalmology images postchemotherapy showing complete resolution of the choroid lesion.

tive plaque therapy may be used for single small to medium-sized tumors.[6]

Systemic chemotherapy is effective in treating ocular metastases especially in chemosensitive tumors such as small cell lung cancer. Several case reports have shown that chemotherapy is efficacious for choroid metastases from non-small cell lung cancer.[7,8] In our case, standard platinum doublet chemotherapy was used as the initial and primary treatment because the patient has other concurrent sites of metastatic disease which require simultaneous attention.

Intravitreal bevacizumab monotherapy has been used to treat choroid metastases.[9,10] Both reports demonstrated anti-angiogenic and antipermeability effects of bevacizumab on the new tumor vessels by fluorescein angiography. These observations suggest the obligate and vital dependence of choroidal tumors on angiogenesis. This forms the rationale for the use of systemic bevacizumab in our patient, apart from the fact that a platinum doublet in combination with bevacizumab is standard therapy in the United States. Furthermore, systemic administration of bevacizumab was chosen over intravitreal injections due to its greater potential to produce effective chemotherapy concentrations around the metastasis via the rich choroidal blood supply which is within the systemic circulation and not protected by the blood-retina barrier.

To our knowledge this is the first case demonstrating that the efficacy and safety of systemic bevacizumab in combination with a platinum doublet for choroid metastasis resulting in symptomatic improvement and durable control of the tumor with minimal ocular or systemic toxicity.

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